



Atty. Dkt. No. 064189-0201 (2924)

1 Fee  
1634

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Heinz-Josef LENZ, et al.

Title: GENOMIC POLYMORPHISM  
FOR PREDICTING  
THERAPEUTIC RESPONSE

Appl. No.: 09/715,764

Filing Date: 11/15/2000

Examiner: Sitton, Jehanne Souaya

Art Unit: 1634

<p><b>CERTIFICATE OF MAILING</b> I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below.</p> <p><u>S. Saito</u> (Printed Name)</p> <p><u>S. Saito</u> (Signature)</p> <p><u>3/3/06</u> (Date of Deposit)</p>
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**TRANSMITTAL**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Transmitted herewith are the following documents for filing in the above-referenced application:

1. Supplemental Information Disclosure Statement (2 pgs.);
2. PTO Form SB/08 (2 pgs.);
3. Twenty (20) references as cited on SB/08 (#4-#23);
4. Return postcard

[ X ] Check number 1585 in the amount of \$180.00 is enclosed.

[ X ] The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise

improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Date March 3, 2006

By Antoinette F. Konski

FOLEY & LARDNER LLP  
Customer Number: 38706  
Telephone: (650) 251-1129  
Facsimile: (650) 856-3710

Antoinette F. Konski  
Attorney for Applicant  
Registration No. 34,202



Atty. Dkt. No. 064189-0201 (2924)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Heinz-Josef LENZ, et al.

Title: GENOMIC POLYMORPHISM FOR  
PREDICTING THERAPEUTIC  
RESPONSE

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**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each non-U.S. patent document and each non-patent document is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

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**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of either a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

**RELEVANCE OF EACH DOCUMENT**

All of the documents are in English.

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

**FEE**

A fee in connection with submission of a supplemental information disclosure statement under 37 CFR §1.97(c) in the amount of \$180.00 in accordance with 37 CFR §1.17(p) is attached.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

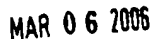
Respectfully submitted,

Date March 3, 2006

By Antoinette F. Konski

FOLEY & LARDNER LLP  
Customer Number: 38706  
Telephone: (650) 251-1129  
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Antoinette F. Konski  
Attorney for Applicant  
Registration No. 34,202



Substitute for form 1449B/PTO

**Date Submitted: March 3, 2006**

*(use as many sheets as necessary)*

Sheet	1	of	3
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**Complete if Known**

<b>Application Number</b>	09/715,764
<b>Filing Date</b>	11/15/2000
<b>First Named Inventor</b>	Heinz-Josef LENZ
<b>Group Art Unit</b>	1634
<b>Examiner Name</b>	Sitton, Jehanne Souaya
<b>Attorney Docket Number</b>	064189-0201 (2924)

[illegible]

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Application Document		Name of Patentee or Applicant of Cited Document	Filing Date of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number	Kind Code <sup>2</sup> (if known)			

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	4		WO 01/36686		University of Southern California	05-25-2001		

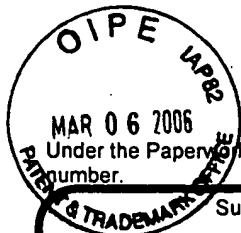
**Examiner  
Signature**

Date  
Considered

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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

Date Submitted: March 3, 2006

(use as many sheets as necessary)

Sheet 2 of 3

**Complete if Known**

Application Number	09/715,764
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First Named Inventor	Heinz-Josef LENZ
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Examiner Name	Sitton, Jehanne Souaya
Attorney Docket Number	064189-0201 (2924)

**FOREIGN PATENT DOCUMENTS**

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	5		WO 01/75175		University of Southern California	10-11-2001		
	6		WO 2004/011625		University of Southern California	02-05-2004		
	7		WO 2004/037852	A2	University of Medicine and Dentistry of New Jersey	05/04/2004		
	8		WO 2004/037852	A3	University of Medicine and Dentistry of New Jersey	05/04/2004		

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	9	ELDER et al. "Thymidylate synthase expression: an independent prognostic factor for local recurrence, distant metastasis, disease-free and overall survival in rectal cancer" <i>Clinical Cancer Res.</i> April 2000, Vol. 6, pages 1378-1384.	
	10	Fox et al. "Angiogenesis in normal tissue adjacent to colon cancer" <i>Journal of Surgical Oncology</i> (Dec. 1998) 69(4):230-234	
	11	IACOPETTA et al. "A polymorphism in the enhancer region of the thymidylate synthase promoter influences the survival of colorectal cancer patients treated with 5-fluorouracil" <i>Brit. J. Cancer</i> Sept. 2001, Vol. 85, No. 6, pages 827-830.	
	12	ISHIKAWA et al. "Dihydropyrimidien dehydrogenase activity and messenger RNA level may be related to the antitumor effect of 5-fluorouracil on human tumor xenografts in nude mice" <i>Clin. Cancer Res.</i> , April 1999, Vol. 5, pages 883-889.	
	13	Kuniyasu et al. "Induction of angiogenesis by hyperplastic colonic mucosa adjacent to colon cancer" <i>American Journal of Pathology</i> (Nov. 2000) 157(5):1523-1535	
	14	LENZ et al. "A 6 base-pair deletion in the 3' UTR of the thymidylate synthase (TS) gene predicts TS mRNA expression in colorectal tumors: a possible candidate gene for colorectal cancer risk" <i>PNAS</i> , March 2002, Vol. 43, page 660 (abstract only).	
	15	Liotta et al. "The microenvironment of the tumour-host interface" <i>Nature</i> (May 2001) 411(6835):375-379	

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SignatureDate  
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	16	PARK et al. "Thymidylate synthase gene polymorphism predicts response to capecitabine in advance colorectal cancer" Int. J. Colorectal Dis., Jan. 2002, Vol. 17, No. 1, pages 46-49.	
	17	PULLARKAT. et al. "Thymidylate synthase gene polymorphism determines response and toxicity of 5-FU chemotherapy" Pharmacogenomics J., 2001, Vol. 1, No. 1, pages 65-70.	
	18	SALONGA et al. "Colorectal tumors responding to 5-fluorouracil have low gene expression levels of dihydropyrimidien dehydrogenase, thymidylate synthase, and thymidine phosphorylase" Clin. Cancer Res., April 2000, Vol. 6, pages 1322-1327.	
	19	SHIROTA et al. "ERCC1 and thymidylate synthase mRNA levels predict survival for colorectal cancer patients receiving combination oxaliplatin and fluorouracil chemotherapy" J. Clin. Oncol., Dec. 2001, Vol. 19, No. 23, pages 4298-4304.	
	20	ULRICH et al. "Searching expressed sequence tag databases: discovery and confirmation of a common polymorphism in the thymidylate synthase gene" Cancer Epidem., Biomarkers and Prevention; American Assoc. Cancer Res., Dec. 2000, Vol. 9, No. 12, pages 1381-1385.	
	21	VILLAFRANCA et al. "Polymorphisms of the repeated sequences in the enhancer region of the thymidylate synthase gene promoter may predict downstaging after preoperative chemoradiation in rectal cancer" J. Clin. Oncol., March 2001, Vol. 19, No. 6, pages 1779-1786.	
	22	EP 03772163.6 Search Report dated 10/24/2005	
	23	EP 03772163.6 Search Report dated 02/03/2006	

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